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Impact of Procalcitonin Testing on Antibiotic Use in Patients Hospitalized With Community-Acquired Pneumonia: A Multi-Hospital Cohort Study

Abhishek Deshpande,[1,2] Rebecca Schulte,[1,3] Ramara E. Walker,[4] Andrea M. Pallotta,[4] Ming Wang,[5] Sameer S. Kadri,[6] Sarah Haessler,[7] Michael Klompas,[8,9] Peter K. Lindenauer,[10,11] and Michael B. Rothberg[1]

[1]Center for Value-Based Care Research, Cleveland Clinic, Cleveland, Ohio, USA; [2]Department of Medical Education, Alice L Walton School of Medicine, Bentonville, Arkansas, USA; [3]Department of Quantitative Health Sciences, Cleveland Clinic, Cleveland, Ohio, USA; [4]Department of Pharmacy, Cleveland Clinic, Cleveland, Ohio, USA; [5]Department of Population and Quantitative Health Sciences, Case Western Reserve University, Cleveland, Ohio, USA; [6]Department of Critical Care Medicine, National Institutes of Health Clinical Center, Bethesda, Maryland, USA; [7]Division of Infectious Diseases, Department of Medicine, University of Massachusetts Chan Medical School-Baystate, Springfield, Massachusetts, USA; [8]Department of Population Medicine, Harvard Medical School and Harvard Pilgrim Health Care Institute, Boston, Massachusetts, USA; [9]Department of Medicine, Brigham and Women's Hospital, Boston, Massachusetts, USA; [10]Department of Healthcare Delivery and Population Sciences, University of Massachusetts Chan Medical School-Baystate, Springfield, Massachusetts, USA; and [11]Department of Medicine, University of Massachusetts Chan Medical School-Baystate, Springfield, Massachusetts, USA

Background. Procalcitonin (PCT) testing may guide antibiotic decisions in community-acquired pneumonia (CAP), but real-world evidence of its impact on antibiotic prescribing in the era of shorter antibiotic courses remains limited.

Methods. We conducted a retrospective cohort study of adults with CAP admitted to the wards of 12 hospitals between November 2022 and January 2025. Primary analyses included: (1) PCT testing rates at admission, (2) the association between PCT testing and duration of antibiotic therapy, and (3) among patients initiated on extended-spectrum antibiotics (ESAs), the relationship between PCT results and early de-escalation. We compared outcomes between PCT-tested and untested patients and between those with low (<0.1 μg/L) vs high (≥0.1 μg/L) PCT values using propensity score overlap weighting to control for potential confounders.

Results. Among 17 290 non–intensive care unit (ICU) admissions for CAP, PCT testing was performed for 10 658 patients (59.5%) within 24 hours of admission. After adjustments, PCT testing was associated with shorter antibiotic duration (adjusted mean difference, −0.32 days; 95% confidence interval [CI], −.52 to −.12) but was not significantly associated with ESA de-escalation compared with no PCT testing (hazard ratio, 1.05; 95% CI, .99–1.12). Patients with low PCT values received shorter antibiotic courses compared with those with high values (adjusted mean difference, −0.56 days; 95% CI, −.85 to −.49).

Conclusions. In non-ICU patients with CAP, PCT testing was associated with modest differences in antibiotic duration, primarily when values were low.

Keywords. procalcitonin; community-acquired pneumonia; antibiotic stewardship; viral pneumonia.

Community-acquired pneumonia (CAP) is a leading cause of hospital admissions in the United States, with >1.5 million adult hospitalizations annually. Respiratory viruses account for more than two-thirds of CAP cases with identified pathogens [1, 2], highlighting the potential importance of distinguishing bacterial from viral pneumonia to reduce unnecessary antibiotic exposure. However, differentiating between these etiologies remains challenging.

Procalcitonin (PCT), an inflammatory biomarker with a quick turnaround time, has shown ability for differentiating between bacterial and viral infections. Procalcitonin levels tend to be higher in bacterial CAP and lower in viral CAP, although with imperfect separation [3]. Previous studies have reported that PCT values ≤0.1 μg/L generally indicate viral infection, whereas values ≥0.25 μg/L suggest bacterial pneumonia [4, 5]. Multiple studies have demonstrated that PCT algorithms and serial measures can reduce antibiotic use while decreasing adverse events [4, 5], and a large patient-level meta-analysis found that PCT reduced antibiotic exposure by ∼3 days without significant differences in adverse outcomes [5].

However, the effectiveness of PCT-guided antibiotic therapy remains controversial. A large randomized controlled trial involving 1656 patients with suspected lower respiratory tract infection found that real-time PCT results did not significantly alter antibiotic management compared with standard care, because physicians often did not act on the results [6]. Current American Thoracic Society/Infectious Diseases Society of America (ATS/IDSA) guidelines do not recommend PCT to guide initiation of antibiotic therapy for patients with CAP

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Correspondence: A. Deshpande, Department of Medical Education, Alice L Walton School of Medicine, 1001 NE J St, Bentonville, AR 72712 (abhishekdp@gmail.com).

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[7] but suggest that low PCT values may help guide antibiotic discontinuation in clinically stable patients who test positive for influenza and show no evidence of bacterial infection [7, 8].

While the number of US acute-care hospitals offering on-site PCT testing has more than doubled in the last decade, approaches to its use vary considerably among institutions and clinicians [9]. Contemporary real-world data on PCT testing practices and their impact on antibiotic utilization remain limited. This study aims to evaluate existing PCT testing practices across multiple hospitals, identify factors associated with PCT testing, and assess its impact on antibiotic prescribing in patients admitted with CAP. Additionally, we evaluated mortality as a safety outcome to ensure that PCT-guided practices do not adversely affect patient outcomes.

METHODS

Study Design and Setting

We conducted a secondary analysis of data that 12 Cleveland Clinic Health System hospitals collected as part of an ongoing 2×2 factorial, cluster-randomized controlled trial [10]. The study protocol for the ongoing RCT has been previously published [10]. The Cleveland Clinic Institutional Review Board approved the study protocol.

Study Population

We included adult patients (aged ≥18 years) admitted through the emergency department with a principal diagnosis of pneumonia between 1 November 2022 and 31 January 2025. We excluded patients (1) transferred from another acute-care facility, (2) discharged from an acute-care hospital in the previous week, (3) diagnosed with cystic fibrosis, (4) admitted to the intensive care unit (ICU) within 24 hours of admission, or (5) who had known pathogens on arrival (defined as positive blood or respiratory cultures in the 72 hours prior to admission).

For the analysis of antibiotic utilization and 30-day mortality, we applied additional exclusions. A detailed description is provided in Supplementary Material 1A.

Data Collection and Variable Definitions

For each hospitalization, we collected demographic data (age, sex, race/ethnicity, and insurance status), clinical presentation characteristics, emergency department diagnosis, vital signs, laboratory values, microbiology results, treatment information, comorbidities, and mortality data from electronic health records. All variables were collected on the day of admission, with comorbidities recorded as present on admission.

We defined severe CAP using 2 established criteria: (1) CURB-65 score ≥3 [11] and (2) modified ATS criteria, defined as having either a major criterion (invasive mechanical ventilation [IMV] or need for vasopressors) or ≥3 minor criteria (high respiratory rate, confusion, uremia, leukopenia, thrombocytopenia, or hypothermia) [7]. Clinical stability at admission was determined retrospectively based on ATS/IDSA criteria and defined as temperature <100°F with no more than 1 sign of clinical instability (systolic blood pressure <90 mmHg, heart rate >100 bpm, respiratory rate >24 breaths/min, or oxygen saturation <90%).

Extended-spectrum antibiotic (ESA) therapy for CAP was defined as drugs that cover methicillin-resistant *Staphylococcus aureus* (MRSA) or *Pseudomonas*. Community-acquired pneumonia antibacterials included a respiratory fluoroquinolone or an antipneumococcal beta-lactam plus a macrolide or doxycycline. A detailed description is provided in Supplementary Materials 1B. Procalcitonin testing was included if ordered within 24 hours of admission, with values dichotomized as low (<0.1 μg/L) or high (≥0.1 μg/L) based on established thresholds [12, 13].

Exposures and Outcomes

We conducted 2 primary group analyses: (1) comparing patients who received PCT testing within 24 hours of admission vs those who did not, and (2) among tested patients, comparing those with low vs high PCT values. The primary outcomes were total antibiotic duration (inpatient and outpatient and measured in days) and time to ESA de-escalation (calculated as hours from the first to last dose of ESA). For the PCT testing comparison only, we also evaluated 30-day all-cause mortality. To maintain consistency with the PCT timeframe, only patients who started on ESA within 24 hours of admission were included in the de-escalation analysis. We evaluated the diagnostic performance of PCT by calculating sensitivity and negative predictive value (NPV) using blood culture positivity as a reference for confirmed bacterial infection. Specificity was not calculated, as the absence of a positive blood culture does not reliably exclude infection, so it was not possible to identify a group of patients without bacterial infection. We also assessed the relationship between PCT levels and the probability of subsequent positive bacterial blood cultures, stratifying results by PCT thresholds.

Statistical Analysis

We summarized categorical variables using frequencies and proportions and continuous variables using means and standard deviations. Group comparisons were performed using 2-sample *t* tests or Wilcoxon rank sum tests for continuous variables and Pearson's χ^2 or Fisher's exact tests for categorical variables, as appropriate. Procalcitonin testing rates and values were compared across hospitals using Pearson's χ^2 test. To address potential confounding, we employed propensity score methods with overlap weighting [14]. A detailed description of the statistical methods is provided in Supplementary Material 1C. We used 2-sided statistical tests with a significance level of 0.05. All analyses were conducted using R version 4.4.0 (R Foundation for Statistical Computing).

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RESULTS

After exclusions, our sample included 17 920 patients with CAP. The mean hospital length of stay was 5.2 ± 4.4 days.

Procalcitonin Testing Patterns

Overall, 59.45% (10 658/17 920) of patients underwent PCT testing within 24 hours of admission. All hospitals performed PCT testing in-house. The median time from sample collection to result availability was 3.75 hours (interquartile range, 1.28–6.45 hours). Testing rates varied substantially across hospitals, ranging from 45.3% to 76.6% ($P < .001$). Among those with PCT tests, 85% had only one test during their hospitalization; 62.1% had high PCT values (≥0.1 μg/L), 37.9% (4055/10 706) had low values (<0.1 μg/L) and 23.2% had very low values (≤0.06 μg/L). Overall, 41% of patients received empiric ESAs at any point, and 25% received them as their first antibiotic. The mean total antibiotic duration was 5.5 ± 3.5 days (median 5 days) for all patients, and the mean total ESA duration was 4.0 ± 2.9 days (median 3 days) among patients who received an ESA.

Table 1 shows patient characteristics by testing status. Patients who underwent PCT testing were slightly older (mean 72 vs 71 years), and there was a higher percentage of females in the PCT group (52% vs 50% in the non-PCT group). Patients who underwent PCT testing had a mean antibiotic duration of 5.4 ± 3.4 days (median 5 days) compared with 5.8 ± 3.5 days (median 5 days) in those without PCT testing. Among patients who received ESAs, mean ESA duration was 3.99 ± 2.89 days (median 3 days) in the PCT group compared with 4.03 ± 2.85 days (median 3 days) in the non-PCT group. In our multivariable logistic regression model (Table 2), factors positively associated with receipt of PCT testing included respiratory culture collection (odds ratio [OR] 1.29, 95% confidence interval [CI], 1.19–1.39), MRSA screening (OR 1.56, 95% CI, 1.45–1.69), COVID-19 positivity (OR 1.86, 95% CI, 1.59–2.19), and valvular disease (OR 1.11, 95% CI, 1.01–1.21). Factors negatively associated with testing included aspiration pneumonia (OR 0.68, 95% CI, .59–.78), HIV (OR 0.69, 95% CI, .47–1.00), and weight loss (OR 0.91, 95% CI, .85–.98). Substantial variation in testing practices was observed across hospitals, with adjusted ORs for testing ranging from 1.11 to 3.92 compared with the reference hospital (Supplementary Table 1).

Clinical Characteristics by Procalcitonin Value

Table 3 shows patient characteristics based on PCT values. Patients with high PCT values (≥0.1 μg/L) demonstrated higher rates of clinical instability (51% vs 32%), bacteremia (7.8% vs 2.3%), as well as longer hospital length of stay (5.6 vs 4.5 days) compared with those with low values. However, patients with high PCT values had lower rates of severe pneumonia as defined ***by CURB-65 scores (17% vs 32%) and ATS criteria (1.1% vs 4.2%). Patients with high PCT also had lower peak white blood cell counts (10.4 vs 13.1 K/μL). Patients with high PCT values had higher rates of both blood culture collection (74% vs 53%) and respiratory culture collection (28% vs 24%). Among those tested, blood culture positivity was 2.3% in the low PCT group vs 7.8% in the high PCT group, while respiratory culture positivity was similar between groups (26% vs 28%, $P = .2$). All comparisons were significant at $P < .001$ except where noted.

Association With Antibiotic Use and Mortality

Table 4 shows the association of PCT testing and PCT values with antibiotic use. After adjustment using overlap weighting, PCT testing was associated with shorter total antibiotic duration by 0.32 days (95% CI, −.52, −.12). Procalcitonin testing was not significantly associated with time to ESA de-escalation compared with no PCT testing (HR 1.05, 95% CI, .99–1.12).

The association between PCT values and antibiotic use was more pronounced. Patients with low PCT values (<0.1 μg/L) received 0.56 days shorter antibiotic courses compared with those with high PCT values (adjusted means: 4.96 vs 5.52 days). However, there was no significant association between PCT values and time to ESA de-escalation (HR 1.08, 95% CI, .94–1.24). Procalcitonin testing showed no significant association with 30-day mortality (OR 0.95, 95% CI, .76–1.18).

Subgroup Analysis

In our prespecified subgroup analysis of patients with laboratory-confirmed viral pneumonia (n = 1420), PCT testing was associated with 0.55 days reduction in antibiotic duration compared with no PCT testing although this did not reach statistical significance (95% CI, −1.12, .02). Among patients with viral pneumonia who underwent PCT testing (n = 979), ~32% (n = 317) had low PCT values (<0.1 μg/L). Those with low PCT values received shorter antibiotic courses than those with high values, with an adjusted difference of 0.17 days (adjusted means: 4.18 vs 4.34 days).

Diagnostic Performance of Procalcitonin

Procalcitonin showed a strong association with bacteremia, with the likelihood of positive blood cultures increasing progressively at higher PCT levels. Using a cutoff of 0.1 μg/L to define an elevated PCT, the test demonstrated a sensitivity of 88.7% and an NPV of 97.7% for detecting positive bacterial blood cultures in patients with CAP. The proportion of patients with bacteremia increased steadily across PCT categories (Table 5): 1.6% among those with very low PCT (≤0.06 μg/L) to 21.2% with PCT >2.5 μg/L. The likelihood of a positive blood culture increased with higher PCT values, with positive likelihood ratios rising from 0.23 at PCT ≤0.05 μg/L to 4.12 at PCT >2.5 μg/L.

DISCUSSION

In this large, multi-hospital retrospective study of almost 18 000 non-ICU patients hospitalized with CAP, we found that

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Table 1. Comparison of the Clinical and Demographic Characteristics of the Entire Cohort and Among Patients Who Were Tested vs Who Were not Tested for Procalcitonin

Characteristic	Overall (N = 17 920)	No PCT (N = 7262)	PCT (N = 10 658)	*P*-Value
Demographics				
Age, mean (*SD*)	72 (16)	71 (16)	72 (16)	<.001
Female sex	9145 (51%)	3636 (50%)	5509 (52%)	.033
Race/ethnicity				<.001
Non-Hispanic White	12 149 (68%)	4848 (67%)	7301 (69%)	
Non-Hispanic Black	4068 (23%)	1812 (25%)	2256 (21%)	
Hispanic	967 (5.4%)	332 (4.6%)	635 (6.0%)	
Other	601 (3.4%)	231 (3.2%)	370 (3.5%)	
Unknown	135 (0.8%)	39 (0.5%)	96 (0.9%)	
Insurance				<.001
Medicare	11 378 (63%)	4579 (63%)	6799 (64%)	
Private	3976 (22%)	1542 (21%)	2434 (23%)	
Medicaid	2044 (11%)	909 (13%)	1135 (11%)	
Other	59 (0.3%)	25 (0.3%)	34 (0.3%)	
Unknown	463 (2.6%)	207 (2.9%)	256 (2.4%)	
Clinical presentation				
ED diagnosis				<.001
Unspecified pneumonia	15 977 (89%)	6421 (88%)	9556 (90%)	
Aspiration pneumonia	925 (5.2%)	488 (6.7%)	437 (4.1%)	
COVID-19 pneumonia	542 (3.0%)	170 (2.3%)	372 (3.5%)	
Influenza pneumonia	153 (0.9%)	58 (0.8%)	95 (0.9%)	
Other viral pneumonia	138 (0.8%)	49 (0.7%)	89 (0.8%)	
Sepsis	185 (1.0%)	76 (1.0%)	109 (1.0%)	
Disease severity indices				
CURB-65, mean (*SD*)	2 (1)	2 (1)	2 (1)	.4
CURB-65 severe	4776 (27%)	1940 (27%)	2836 (27%)	.9
ATS severe pneumonia[a]	546 (3.1%)	227 (3.2%)	319 (3.0%)	.6
Confusion	366 (2.0%)	137 (1.9%)	229 (2.1%)	.2
Stability on day 1				.2
Stable	10 017 (56%)	4016 (55%)	6001 (56%)	
Unstable	7902 (44%)	3245 (45%)	4657 (44%)	
Vital signs[b]				
SBP minimum, mmHg	115 (21)	114 (21)	115 (21)	<.001
DBP minimum, mmHg	67 (14)	67 (14)	67 (14)	.079
Respiratory rate maximum	24.9 (6.0)	24.8 (6.2)	24.9 (5.9)	.008
Pulse maximum, bpm	102 (20)	102 (21)	101 (20)	.036
Temperature maximum, °F	98.95 (1.37)	98.99 (1.41)	98.93 (1.35)	.11
SPO_2 minimum, %	92.1 (4.5)	92.2 (4.6)	92.1 (4.5)	.004
Laboratory values[c]				
WBC count maximum, K/μL	12.3 (8.1)	12.5 (8.4)	12.1 (8.0)	<.001
Hemoglobin maximum, g/dL	12.32 (2.26)	12.33 (2.31)	12.31 (2.22)	.7
Na maximum, mEq/L	138.2 (4.2)	138.2 (4.4)	138.2 (4.2)	.7
BUN maximum, mg/dL	24 (16)	24 (17)	24 (16)	.4
Glucose maximum, mg/dL	166 (83)	164 (82)	168 (83)	<.001
Albumin maximum, g/dL	3.69 (0.51)	3.69 (0.53)	3.69 (0.50)	>.9
Microbiology				
Blood cultures[d]				
Obtained	11 721 (65%)	4681 (64%)	7040 (66%)	.028
Positive	752 (6.4%)	319 (6.8%)	433 (6.2%)	.2
Respiratory cultures[d]				<.001
Obtained	4357 (24%)	1546 (21%)	2811 (26%)	
Positive	1210 (28%)	432 (28%)	778 (28%)	.9
MRSA screening	5018 (28%)	1673 (23%)	3345 (31%)	<.001
Viral testing				
COVID-19 positive	1291 (7.2%)	385 (5.3%)	906 (8.5%)	<.001
Influenza positive	327 (1.8%)	111 (1.5%)	216 (2.0%)	.014
RSV positive	242 (1.4%)	76 (1.0%)	166 (1.6%)	.004

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Table 1. Continued

Characteristic	Overall (N = 17 920)	No PCT (N = 7262)	PCT (N = 10 658)	*P*-Value
Treatments and interventions				
Vasopressors on day 1	30 (0.2%)	17 (0.2%)	13 (0.1%)	.071
Noninvasive ventilation	923 (5.2%)	363 (5.0%)	560 (5.3%)	.4
IMV	14 (<0.1%)	7 (<0.1%)	7 (<0.1%)	.5
Dialysis	696 (3.9%)	303 (4.2%)	393 (3.7%)	.10
Comorbidities				
Immunocompromised	1484 (8.3%)	629 (8.7%)	855 (8.0%)	.13
Cardiovascular				
Hypertension	13 668 (76%)	5394 (74%)	8274 (78%)	<.001
Heart failure	6312 (35%)	2383 (33%)	3929 (37%)	<.001
Peripheral vascular disease	4364 (24%)	1613 (22%)	2751 (26%)	<.001
Valvular disease	3193 (18%)	1193 (16%)	2000 (19%)	<.001
Pulmonary circulation disorders	1882 (11%)	733 (10%)	1149 (11%)	.14
Pulmonary disease	9879 (55%)	3827 (53%)	6052 (57%)	<.001
Endocrine				
Diabetes without complications	5987 (33%)	2326 (32%)	3661 (34%)	.001
Diabetes with complications	4590 (26%)	1721 (24%)	2869 (27%)	<.001
Hypothyroidism	4095 (23%)	1484 (20%)	2611 (24%)	<.001
Obesity	4785 (27%)	1786 (25%)	2999 (28%)	<.001
Neurologic				
Other neurological disorders	6388 (36%)	2596 (36%)	3792 (36%)	.8
Paralysis	1011 (5.6%)	442 (6.1%)	569 (5.3%)	.033
Gastrointestinal/hepatic				
Liver disease	2476 (14%)	969 (13%)	1507 (14%)	.13
Chronic peptic ulcer disease	1099 (6.1%)	432 (5.9%)	667 (6.3%)	.4
Renal/metabolic				
Renal failure	5736 (32%)	2200 (30%)	3536 (33%)	<.001
Fluid/electrolyte disorders	11 027 (62%)	4350 (60%)	6677 (63%)	<.001
Hematologic				
Deficiency anemias	9028 (50%)	3522 (48%)	5506 (52%)	<.001
Blood loss anemia	1509 (8.4%)	568 (7.8%)	941 (8.8%)	.017
Coagulation deficiency	3228 (18%)	1206 (17%)	2022 (19%)	<.001
Oncologic				
Solid tumor	4690 (26%)	1849 (25%)	2841 (27%)	.074
Metastatic cancer	2057 (11%)	811 (11%)	1246 (12%)	.3
Lymphoma	734 (4.1%)	262 (3.6%)	472 (4.4%)	.006
Psychiatric				
Depression	4253 (24%)	1625 (22%)	2628 (25%)	<.001
Psychoses	2657 (15%)	1049 (14%)	1608 (15%)	.2
Drug abuse	2338 (13%)	1015 (14%)	1323 (12%)	.002
Alcohol abuse	1502 (8.4%)	670 (9.2%)	832 (7.8%)	<.001
Other				
Weight loss	7193 (40%)	2934 (40%)	4259 (40%)	.6
HIV	128 (0.7%)	66 (0.9%)	62 (0.6%)	.011

Data are presented as n (%) for categorical variables and mean (*SD*) for continuous variables unless otherwise specified.

Abbreviations: ATS, American Thoracic Society; BP, blood pressure; BUN, blood urea nitrogen; DBP, diastolic blood pressure; ED, emergency department; IMV, invasive mechanical ventilation; MRSA, methicillin-resistant *Staphylococcus aureus*; PCT, procalcitonin; RSV, respiratory syncytial virus; *SD*, standard deviation; SBP, systolic blood pressure; WBC, white blood cell.

[a]Two hundred and two patients had missing data for ATS severe pneumonia assessment.

[b]Data available for vital signs: SBP (N = 17 888), DBP (N = 17 871), respiratory rate (N = 17 719), pulse (N = 17 911), temperature (N = 17 786), and SpO_2 (N = 17 865).

[c]Data available for laboratory values: BUN (N = 17 903), WBC (N = 17 908), Na (N = 17 909), hemoglobin (N = 17 910), glucose (N = 17 915), and albumin (N = 16 906).

[d]Culture results shown as number positive/number tested. Missing culture data (not obtained): respiratory cultures (N = 13 563) and blood cultures (N = 6199).

nearly 60% of patients underwent PCT testing within 24 hours of admission, with substantial variation across the 12 participating hospitals. Procalcitonin testing was associated with modest but statistically significant differences in antibiotic duration with no negative impact on 30-day mortality. Low PCT values (<0.1 μg/L) were associated with slightly shorter antibiotic courses compared with high values, suggesting that clinicians may have incorporated test results into their

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Table 2. Multivariable Logistic Regression Model for Procalcitonin Testing

Characteristic	Odds Ratio (95% CI)	*P*-Value
Demographics		
Age (per year)	1.00 (1.00–1.01)	.04
Male sex	0.98 (.91–1.05)	.50
Race/ethnicity (ref: Non-Hispanic White)		
Non-Hispanic Black	1.05 (.95–1.15)	.34
Hispanic	1.19 (1.02–1.39)	.03
Other	0.98 (.82–1.18)	.86
Unknown	1.50 (1.01–2.27)	.05
Insurance (ref: private)		
Medicaid	0.90 (.80–1.02)	.10
Medicare	0.94 (.86–1.02)	.13
Other	0.82 (.47–1.44)	.47
Unknown	0.88 (.72–1.09)	.24
Clinical presentation		
ED diagnosis (ref: unspecified pneumonia)		
Aspiration pneumonia	0.68 (.59–.78)	<.001
COVID-19 pneumonia	0.87 (.68–1.11)	.26
Influenza pneumonia	1.00 (.70–1.43)	.99
Other viral pneumonia	0.93 (.63–1.39)	.74
Sepsis	1.02 (.75–1.40)	.89
Disease severity indices		
CURB-65 score (per point)	0.97 (.92–1.02)	.26
ATS severe	0.98 (.80–1.20)	.82
Confusion	1.22 (.96–1.56)	.11
Unstable on day 1	0.92 (.85–.99)	.03
Vital signs		
SBP minimum (per mmHg)	1.00 (1.00–1.01)	<.001
DBP minimum (per mmHg)	1.00 (1.00–1.00)	.64
Respiratory rate maximum (per breath/min)	1.01 (1.00–1.01)	.09
Laboratory values		
WBC maximum (K/μL)	0.99 (.99–1.00)	.005
BUN maximum	1.00 (1.00–1.00)	.48
Na maximum	1.00 (.99–1.01)	.70
Glucose maximum	1.00 (1.00–1.00)	.45
Hemoglobin maximum	1.01 (.99–1.02)	.56
SPO_2 minimum (per %)	1.00 (.99–1.00)	.20
Microbiology and testing		
Blood culture obtained	1.03 (.96–1.11)	.42
Respiratory culture obtained	1.29 (1.19–1.39)	<.001
MRSA screening	1.56 (1.45–1.69)	<.001
COVID-19 positive	1.86 (1.58–2.19)	<.001
Influenza positive	1.38 (1.07–1.78)	.01
RSV positive	1.61 (1.19–2.20)	.003
Treatments and interventions		
Vasopressors on day 1	0.68 (.29–1.55)	.36
Noninvasive ventilation	0.99 (.85–1.15)	.88
IMV	0.69 (.22–2.18)	.52
Dialysis	0.84 (.70–1.00)	.06
Comorbidities		
Cardiovascular		
Hypertension	1.04 (.95–1.13)	.39
Heart failure	1.08 (1.00–1.17)	.06
Peripheral vascular disease	1.07 (.99–1.16)	.11
Valvular disease	1.11 (1.01–1.21)	.03
Pulmonary circulation disorders	1.04 (.93–1.15)	.51
Pulmonary disease	1.08 (1.01–1.16)	.03
Endocrine		

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Table 2. Continued

Characteristic	Odds Ratio (95% CI)	*P*-Value
Diabetes without complications	0.94 (.85–1.05)	.28
Diabetes with complications	1.07 (.96–1.20)	.23
Hypothyroidism	1.13 (1.04–1.22)	.003
Obesity	1.03 (.95–1.12)	.41
Neurologic		
Other neurological disorders	0.98 (.91–1.05)	.50
Paralysis	0.97 (.84–1.11)	.63
Gastrointestinal/hepatic		
Liver disease	0.98 (.89–1.08)	.71
Chronic peptic ulcer disease	0.96 (.84–1.10)	.54
Renal/metabolic		
Renal failure	1.03 (.94–1.12)	.55
Fluid/electrolyte disorders	0.98 (.91–1.05)	.52
Hematologic		
Deficiency anemias	1.02 (.94–1.10)	.62
Blood loss anemia	1.02 (.90–1.15)	.75
Coagulation deficiency	1.02 (.93–1.12)	.69
Oncologic		
Solid tumor	1.00 (.92–1.09)	.96
Metastatic cancer	0.98 (.87–1.09)	.68
Lymphoma	1.16 (.98–1.37)	.08
Psychiatric		
Depression	1.03 (.95–1.12)	.51
Psychoses	1.03 (.93–1.14)	.57
Drug abuse	0.97 (.87–1.08)	.58
Alcohol abuse	0.92 (.81–1.04)	.17
Other		
Weight loss	0.91 (.85–.98)	.01
HIV	0.69 (.47–1.00)	.05

Results from multivariable logistic regression model predicting PCT testing. The model excludes albumin due to missing data and one encounter with WBC <300.

Abbreviations: ATS, American Thoracic Society; BUN, blood urea nitrogen; CI, confidence interval; DBP, diastolic blood pressure; ED, emergency department; MRSA, methicillin-resistant *Staphylococcus aureus*; PCT, procalcitonin; RSV, respiratory syncytial virus; SBP, systolic blood pressure; WBC, white blood cell.

treatment decisions. However, PCT testing was not associated with early de-escalation of ESAs.

Our findings demonstrate the more modest association of PCT testing in routine clinical practice. Randomized trials have reported larger reductions in antibiotic durations, but baseline antibiotic courses were substantially longer in these trials compared with current practice in study hospitals. For example, a meta-analysis of randomized trials, including 2910 patients with CAP, reported that PCT algorithms reduced antibiotic duration by 2.5 days (95% CI, −2.02 to −2.87) compared with standard of care [5], whereas we found PCT testing was associated with only 0.32 days shorter duration.

This difference likely reflects several factors. First, ProHOSP and other similar European randomized trials used prescriptive PCT-guided algorithms that required antibiotic decisions based on PCT results, while the Huang et al US trial, which took a less prescriptive approach similar to our real-world setting, showed minimal impact [6, 15]. In our study, physicians ordered PCT at their discretion and interpreted results without a formal protocol.

Second, baseline antibiotic durations have decreased substantially since earlier RCTs. Previous trials reported mean durations of 8 days in PCT groups and 10.5 days in control groups [5], whereas our study observed mean durations of only 5.5 days overall, with 5.4 days in the PCT group and 5.8 days in the non-PCT group. When comparing patients with low vs high PCT values, we observed mean durations of 4.96 days and 5.52 days, respectively, a difference of 0.56 days. This shorter baseline duration reflects implementation of the 2019 ATS/IDSA guidelines recommending 5 days of therapy for clinically stable patients [7] and evidence supporting shorter courses [16], leaving limited opportunity for further reductions.

The modest impact of low PCT values on antibiotic duration raises important questions about clinical decision-making. In the overall cohort, low PCT values were associated with only 0.56 days shorter duration, and even in patients with confirmed viral pneumonia, the difference was just 0.17 days. Surprisingly, only one-third of patients with laboratory-confirmed viral pneumonia had low PCT values (<0.1 μg/L). However, given that 66% of our total cohort had values <0.25 μg/L, utilizing this higher threshold as recommended by some algorithms

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Table 3. Comparison of the Clinical and Demographic Characteristics of the Entire Cohort and Among Patients With Low Procalcitonin Value vs Those With High Procalcitonin Value

Characteristic	Overall (N = 10 658)	Low PCT (<0.1) (N = 4039)	High PCT (≥0.1) (N = 6619)	*P*-Value
Demographics				
Age, mean (*SD*)	72 (16)	72 (17)	73 (15)	.008
Gender				<.001
Female	5509 (52%)	2379 (59%)	3130 (47%)	
Male	5149 (48%)	1660 (41%)	3489 (53%)	
Race/ethnicity				.5
Non-Hispanic White	7301 (69%)	2751 (68%)	4550 (69%)	
Non-Hispanic Black	2256 (21%)	853 (21%)	1403 (21%)	
Hispanic	635 (6.0%)	241 (6.0%)	394 (6.0%)	
Other	370 (3.5%)	156 (3.9%)	214 (3.2%)	
Unknown	96 (0.9%)	38 (0.9%)	58 (0.9%)	
Insurance				<.001
Medicare	6799 (64%)	2506 (62%)	4293 (65%)	
Private	2434 (23%)	909 (23%)	1525 (23%)	
Medicaid	1135 (11%)	516 (13%)	619 (9.4%)	
Other	34 (0.3%)	13 (0.3%)	21 (0.3%)	
Unknown	256 (2.4%)	95 (2.4%)	161 (2.4%)	
Clinical presentation				
ED diagnosis				<.001
Unspecified pneumonia	9556 (90%)	3686 (91%)	5870 (89%)	
Aspiration pneumonia	437 (4.1%)	161 (4.0%)	276 (4.2%)	
COVID-19 pneumonia	372 (3.5%)	114 (2.8%)	258 (3.9%)	
Influenza pneumonia	95 (0.9%)	26 (0.6%)	69 (1.0%)	
Other viral pneumonia	89 (0.8%)	33 (0.8%)	56 (0.8%)	
Sepsis	109 (1.0%)	19 (0.5%)	90 (1.4%)	
Disease severity indices				
CURB-65, mean (*SD*)	2 (1)	2 (1)	2 (1)	<.001
CURB-65 severe	2836 (27%)	685 (17%)	2151 (32%)	<.001
ATS severe[a]	319 (3.0%)	42 (1.1%)	277 (4.2%)	<.001
Confusion	229 (2.1%)	87 (2.2%)	142 (2.1%)	>.9
Stability on day 1				<.001
Stable	6001 (56%)	2746 (68%)	3255 (49%)	
Unstable	4657 (44%)	1293 (32%)	3364 (51%)	
Vital signs[b]				
SBP minimum, mmHg	115 (21)	119 (20)	113 (21)	<.001
DBP minimum, mmHg	67 (14)	65 (14)	69 (15)	<.001
Respiratory rate maximum	24.9 (5.9)	24.2 (5.5)	25.3 (6.1)	<.001
Pulse maximum, bpm	101 (20)	98 (20)	104 (20)	<.001
Temperature maximum, °F	98.93 (1.35)	98.53 (1.00)	99.17 (1.47)	<.001
SPO_2 minimum, %	92.1 (4.5)	92.4 (4.3)	91.9 (4.5)	<.001
Laboratory values[c]				
WBC counts maximum, K/μL	12.1 (8.0)	10.4 (6.6)	13.1 (8.5)	<.001
Hemoglobin maximum, g/dL	12.31 (2.22)	12.73 (2.02)	12.06 (2.29)	<.001
Na maximum, mEq/L	138.2 (4.2)	139.0 (3.7)	137.7 (4.3)	<.001
BUN maximum, mg/dL	24 (16)	18 (9)	27 (18)	<.001
Glucose maximum, mg/dL	168 (83)	161 (78)	172 (85)	<.001
Albumin maximum, g/dL	3.69 (0.50)	3.84 (0.42)	3.60 (0.52)	<.001
Microbiology				
Blood cultures[d]				<.001
Obtained	7040 (66%)	2141 (53%)	4899 (74%)	
Positive	433 (6.2%)	49 (2.3%)	384 (7.8%)	
Respiratory cultures[d]				<.001
Obtained	2811 (26%)	956 (24%)	1855 (28%)	
Positive	778 (28%)	251 (26%)	527 (28%)	.2
MRSA screening	3345 (31%)	1031 (26%)	2314 (35%)	<.001

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Table 3. Continued

Characteristic	Overall (N = 10 658)	Low PCT (<0.1) (N = 4039)	High PCT (≥0.1) (N = 6619)	*P*-Value
Viral testing				
COVID-19 positive	906 (8.5%)	304 (7.5%)	602 (9.1%)	.005
Influenza positive	216 (2.0%)	50 (1.2%)	166 (2.5%)	<.001
RSV positive	166 (1.6%)	55 (1.4%)	111 (1.7%)	.2
Treatments and interventions				
Vasopressors on day 1	13 (0.1%)	3 (<0.1%)	10 (0.2%)	.4
Noninvasive ventilation	560 (5.3%)	199 (4.9%)	361 (5.5%)	.2
IMV	7 (<0.1%)	2 (<0.1%)	5 (<0.1%)	.7
Dialysis	393 (3.7%)	5 (0.1%)	388 (5.9%)	<.001
Comorbidities				
Immunocompromised	855 (8.0%)	227 (5.6%)	628 (9.5%)	<.001
Cardiovascular				
Hypertension	8274 (78%)	3141 (78%)	5133 (78%)	.8
Heart failure	3929 (37%)	1479 (37%)	2450 (37%)	.7
Peripheral vascular disease	2751 (26%)	951 (24%)	1800 (27%)	<.001
Valvular disease	2000 (19%)	742 (18%)	1258 (19%)	.4
Pulmonary circulation disorders	1149 (11%)	427 (11%)	722 (11%)	.6
Pulmonary disease	6052 (57%)	2543 (63%)	3509 (53%)	<.001
Endocrine				
Diabetes without complications	3661 (34%)	1301 (32%)	2360 (36%)	<.001
Diabetes with complications	2869 (27%)	977 (24%)	1892 (29%)	<.001
Hypothyroidism	2611 (24%)	990 (25%)	1621 (24%)	>.9
Obesity	2999 (28%)	1251 (31%)	1748 (26%)	<.001
Neurologic				
Other neurological disorders	3792 (36%)	1466 (36%)	2326 (35%)	.2
Paralysis	569 (5.3%)	231 (5.7%)	338 (5.1%)	.2
Gastrointestinal/hepatic				
Liver disease	1507 (14%)	562 (14%)	945 (14%)	.6
Chronic peptic ulcer disease	667 (6.3%)	247 (6.1%)	420 (6.3%)	.6
Renal/metabolic				
Renal failure	3536 (33%)	926 (23%)	2610 (39%)	<.001
Fluid/electrolyte disorders	6677 (63%)	2387 (59%)	4290 (65%)	<.001
Hematologic				
Deficiency anemias	5506 (52%)	1825 (45%)	3681 (56%)	<.001
Blood loss anemia	941 (8.8%)	293 (7.3%)	648 (9.8%)	<.001
Coagulation deficiency	2022 (19%)	588 (15%)	1434 (22%)	<.001
Oncologic				
Solid tumor	2841 (27%)	925 (23%)	1916 (29%)	<.001
Metastatic cancer	1246 (12%)	375 (9.3%)	871 (13%)	<.001
Lymphoma	472 (4.4%)	126 (3.1%)	346 (5.2%)	<.001
Psychiatric				
Depression	2628 (25%)	1082 (27%)	1546 (23%)	<.001
Psychoses	1608 (15%)	706 (17%)	902 (14%)	<.001
Drug abuse	1323 (12%)	546 (14%)	777 (12%)	.007
Alcohol abuse	832 (7.8%)	366 (9.1%)	466 (7.0%)	<.001
Other				
Weight loss	4259 (40%)	1480 (37%)	2779 (42%)	<.001
HIV	62 (0.6%)	21 (0.5%)	41 (0.6%)	.5

Data are presented as n (%) for categorical variables and mean (*SD*) for continuous variables. *P*-values calculated using Wilcoxon rank sum test, Pearson's χ^2 test, or Fisher's exact test as appropriate.

Abbreviations: ATS, American Thoracic Society; BP, blood pressure; BUN, blood urea nitrogen; DBP, diastolic blood pressure; ED, emergency department; MRSA, methicillin-resistant *Staphylococcus aureus*; PCT, procalcitonin; RSV, respiratory syncytial virus; *SD,* standard deviation; SBP, systolic blood pressure; WBC, white blood cell.

[a]One hundred and seventeen patients had missing data for ATS severe pneumonia assessment.

[b]Missing data for vital signs: SBP/DBP (n = 17/29), respiratory rate (n = 98), pulse (n = 4), temperature (n = 68), and SpO_2 (n = 30).

[c]Laboratory testing completed in all patients except albumin (missing n = 537).

[d]Culture results shown as number positive/number tested (%).

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Table 4. Impact of Procalcitonin Testing and Procalcitonin Values on Antibiotic Use: Primary and Sensitivity Analyses

Outcome	Comparison	N	Effect Estimate (95% CI)[a]	*P*-Value
PCT testing				
Total antibiotic duration	PCT vs No PCT	13 211	−0.32 (−.52, −.12)	.002
Time to ESA de-escalation[b]	PCT vs No PCT	4558	HR: 1.05 (.99, 1.12)	.11
30-Day mortality	PCT vs No PCT	13 211	OR: 0.95 (.76, 1.18)	.6
PCT value				
Total antibiotic duration	Low vs High PCT[c]	8000	−0.56 (4.96 vs 5.52)[d]	<.001
Time to ESA de-escalation[b]	Low vs High PCT[c]	2784	HR: 1.08 (.94, 1.24)	.2
Sensitivity analyses: patients with viral pneumonia[d]				
PCT testing (n = 1420)				
Total antibiotic duration	PCT vs No PCT	1373	−0.55 (−1.12, .02)	.06
Time to ESA de-escalation	PCT vs No PCT	362	HR: 1.30 (1.00, 1.68)	.049
PCT value (n = 979)				
Total antibiotic duration	Low vs High PCT[c]	979	−0.16 (4.18 vs 4.34)[d]	.7
Time to ESA de-escalation[b]	Low vs High PCT[c]	265	HR: 0.81 (.57, 1.17)	.3

Abbreviations: CI, confidence interval; ESA, extended-spectrum antibiotics; HR, hazard ratio; NA, not applicable; PCT, procalcitonin.

[a]All estimates derived from overlap weighted regression models.

[b]ESA duration analyzed using overlap weighted Cox proportional hazards model. For linear regression estimates, negative values indicate reduction in duration. For HRs, values >1 indicate shorter time to event.

[c]Low PCT defined as <0.1, high PCT defined as ≥0.1.

[d]Viral pneumonia defined as positive COVID/Flu/RSV test (9.2% of PCT testing group).

Table 5. Association Between Procalcitonin Levels and Blood Culture Results

PCT Range (μg/L)	Negative Blood Culture, n (%)	Positive Blood Culture, n (%)
≤0.06 μg/L	1223 (98.4)	20 (1.6)
0.06–0.1 μg/L	869 (96.8)	29 (3.2)
0.1–0.25 μg/L	2018 (96.7)	69 (3.3)
0.25–0.5 μg/L	902 (95.5)	42 (4.5)
0.5–0.75 μg/L	348 (92.1)	30 (7.9)
0.75–1.0	216 (90.8)	22 (9.2)
1.0–2.5	440 (88.0)	60 (12.0)
>2.5	597 (78.8)	161 (21.2)
Total	6639 (93.9)	434 (6.1)

would likely identify a majority of these viral patients as candidates for de-escalation. It is possible that elevated values >0.1 μg/L in this group may reflect inflammatory responses rather than bacterial co-infection [17]. These findings suggest multiple barriers to PCT-guided antibiotic reduction: physicians may continue antibiotics despite low PCT values due to clinical uncertainty, concerns about bacterial co-infection, or institutional culture, while elevated PCT values in viral pneumonia may paradoxically prompt extended therapy. This bidirectional effect, where low values have limited impact and high values may increase use even in viral cases, may help explain the modest overall impact on antibiotic utilization. Further research examining the distribution of antibiotic durations and factors influencing discontinuation decisions across different PCT values and clinical scenarios could inform more effective implementation strategies. Even if all patients with low PCT values (38% of those tested) had received no antibiotics, the maximum achievable reduction would be <2 days, suggesting that physicians incorporate PCT results as one factor among many rather than as a definitive decision tool.

Finally, most RCTs utilized serial PCT measurements to guide antibiotic decisions, whereas 85% of our patients had only a single PCT measurement on admission. Current guidelines suggest serial PCT measurements may be beneficial when the average length of stay exceeds 5–7 days [7]. With most of our patients discharged within 5 days, serial measurements may be less relevant in contemporary practice.

Procalcitonin testing was not associated with time to ESA de-escalation. While clinical guidelines suggest that a low PCT value can help guide early antibiotic discontinuation for patients with a positive test for influenza and no evidence of bacterial infection, they do not address de-escalation of ESA in relation to PCT. This is conceivable given that PCT yields no information on antimicrobial resistance. Clinicians often continue ESAs despite low PCT results because of clinical severity, structural lung disease, or history of infection with resistant

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organisms, risks that PCT cannot rule out. In a large multicenter study of 179 US hospitals, we previously reported that prolonged antibiotic courses are frequently administered to patients with confirmed viral pneumonia, suggesting a widespread practice pattern [18]. Our findings indicate that PCT testing may be more effective at influencing total antibiotic duration than altering the timing of antibiotic de-escalation.

Our analysis of PCT's diagnostic performance showed a strong correlation with bacteremia risk, with a sensitivity of 88.7% and an NPV of 97.7% using blood culture as a reference standard. This is in agreement with previous observational studies that have reported sensitivity of ~88% for PCT using blood culture as a gold standard [19]. In our study, the likelihood of positive blood cultures increased progressively with higher PCT levels. The positive likelihood ratio rose from 0.23 at PCT ≤0.05 μg/L to 4.12 at PCT >2.5 μg/L. Our findings support the utility of PCT in risk stratification, particularly for identifying patients at low risk of bacteremia who might safely receive shorter courses of antibiotics.

Our study has several limitations. First, as a retrospective analysis, there may have been unmeasured confounders influencing PCT testing decisions and antibiotic prescribing, but the fact that low PCT levels accounted for all the reduction in antibiotics suggests that healthcare teams respond to the test appropriately. Second, the substantial variation in PCT testing rates across hospitals suggests institutional cultures and differences that may affect generalizability. Third, we lacked specific criteria for antibiotic de-escalation decisions and could not verify adherence to any PCT-guided algorithm, as testing interpretation was at the discretion of individual clinicians. Fourth, the diagnostic performance values apply only to patients with blood culture–confirmed bacterial CAP and may not be generalized to the broader population of patients hospitalized for pneumonia, most of whom do not have positive blood cultures. Finally, our focus on immunocompetent adults with non-ICU CAP limits the generalizability of our conclusions to other patient populations.

Our findings have implications for PCT use in non-ICU patients with CAP. The modest overall effect suggests that PCT testing alone, without an algorithm or other guidance, may have limited impact on antibiotic prescribing. As previously suggested, a more selective approach, focused on testing patients with low pretest probability of bacterial pneumonia and a favorable comorbidity profile, might yield greater benefits [20]. In these patients, low PCT values could provide support for even earlier discontinuation. This is in agreement with the current ATS/IDSA guidelines, which recommend PCT primarily for guiding antibiotic discontinuation rather than initiation [7].

In conclusion, this multi-hospital observational study demonstrates that PCT testing in non-ICU patients admitted with CAP was associated with modest but significant reductions in antibiotic duration, particularly in patients with low PCT values. Our findings, derived from real-world practice, demonstrate both the potential utility and challenges of PCT-guided antibiotic stewardship.

Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

Author contributions. Study concept and design: A. D., M. B. R., R. W., A. M. P., M. W., S. S. K., M. K., and P. K. L. Acquisition, analysis, or interpretation of the data and critical revision of the manuscript: all authors. Drafting of the manuscript: A. D., R. S., M. W., and M. B. R. Statistical analysis: R. S., A. D., M. B. R., and M. W. All authors approved the final draft of the manuscript. A. D. takes responsibility for the content of the manuscript, including the data and its analysis.

Data availability. Data may be available from the corresponding author upon reasonable request and after execution of a data use agreement with Cleveland Clinic.

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